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### Prioritising prevention strategies for patients in antiretroviral treatment programmes in resource-limited settings

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## Prioritising prevention strategies for patients in antiretroviral treatment programmes in resource-limited settings

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Expanded access to antiretroviral therapy (ART) offers opportunities to strengthen HIV prevention in resource-limited settings. We invited 27 ART programmes from urban settings in Africa, Asia and South America to participate in a survey, with the aim to examine what preventive services had been integrated in ART programmes. Twenty-two programmes participated; eight (36%) from South Africa, two from Brazil, two from Zambia and one each from Argentina, India, Thailand, Botswana, Ivory Coast, Malawi, Morocco, Uganda and Zimbabwe and one occupational programme of a brewery company included five countries (Nigeria, Republic of Congo, Democratic Republic of Congo, Rwanda and Burundi). Twenty-one sites (96%) provided health education and social support, and 18 (82%) provided HIV testing and counselling. All sites encouraged disclosure of HIV infection to spouses and partners, but only 11 (50%) had a protocol for partner notification. Twenty-one sites (96%) supplied male condoms, seven (32%) female condoms and 20 (91%) provided prophylactic ART for the prevention of mother-to-child transmission. Seven sites (33%) regularly screened for sexually transmitted infections (STI). Twelve sites (55%) were involved in activities aimed at women or adolescents, and 10 sites (46%) in activities aimed at serodiscordant couples. Stigma and discrimination, gender roles and funding constraints were perceived as the main obstacles to effective prevention in ART programmes. We conclude that preventive services in ART programmes in lower income countries focus on health education and the provision of social support and male condoms. Strategies that might be equally or more important in this setting, including partner notification, prompt diagnosis and treatment of STI and reduction of stigma in the community, have not been implemented widely.

**Keywords:** HIV/AIDS; antiretroviral therapy; prevention; partner notification; serodiscordant couples

### Introduction

HIV prevention efforts in high-income and low-income settings have traditionally focused on reducing the risk of HIV infection among HIV-negative individuals or in populations with unknown serostatus, and concerns about stigma and negative social outcomes related to knowledge of HIV status have been paramount (Bunnell, Mermin, & De Cock, 2006). HIV testing services were not widely available, particularly in resource-limited settings. This situation has changed in recent years with the scaling-up of antiretroviral therapy (ART) and HIV testing in low and middle-income countries. Close to four million people with

HIV/AIDS were estimated to be receiving treatment at the end of 2008 (World Health Organization (WHO), 2009). Adherence to ART (Mills et al., 2006) and immunological and virological response (Braitstein et al., 2006; Keiser et al., 2008b) in resource-limited countries equal or exceed that in high-income settings, and a decline in mortality at the population level has recently been observed in Malawi and South Africa (Egger & Boule, 2008; Jahn et al., 2008).

The scale-up of ART in resource-limited settings is a major achievement, which is extending the lives of many people with HIV/AIDS. It is however clear that “we cannot treat our way out of this epidemic”: in the

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absence of reductions in HIV incidence, ART programmes will not be able to keep up with the increasing number of people in urgent need of treatment (De Cock, 2006). The Global HIV Prevention Working Group, a panel of public health experts, clinicians, researchers and people affected by HIV/AIDS, the WHO and other agencies have argued that expanded access to ART offers new opportunities to strengthen HIV prevention (Gayle & Lange, 2004; WHO, 2008b). It is unclear to what extent preventive services have been integrated in ART programmes in resource-limited settings. We addressed this question in a survey of treatment sites in Africa, Asia and South America.

## Methods

We conducted an electronic survey of the 27 programmes that provide ART to adult patients in 13 countries in Africa, Asia and Latin America and participate in the ART in Lower Income Countries (ART-LINC) collaboration, which is part of the International epidemiological Databases to Evaluate AIDS (IeDEA). The collaboration has been described in detail elsewhere (Dabis et al., 2005; Keiser et al., 2008a). Briefly, it was set up in 2003 with the aims of defining the prognosis of HIV-infected patients treated with ART in resource-limited settings and to compare the experience between different settings, delivery modes and types of monitoring. Potentially eligible sites were identified in 2003 by screening abstracts of international conferences, performing MEDLINE searches and through personal contacts. A total of 31 centres were contacted. To be eligible, centres needed to prospectively collect information on patients treated with ART. The ethics committees or institutional review boards of all participating sites approved participation in ART-LINC of IeDEA.

### *Questionnaire development, testing and implementation*

The study was discussed with the Steering Committee of ART-LINC, and all collaborators were invited to comment on draft questionnaires. Item generation involved the compilation of a comprehensive list of relevant recommendations on HIV-prevention in HIV-infected people ("positive prevention"). We performed searches in MEDLINE (Pubmed version) without language restrictions to identify relevant articles in May 2007 and updated searches in July 2008. We checked the citations to five key articles (Allen et al., 1992; Kalichman et al., 2001; Marks, Burris, & Peterman, 1999; Oxman et al., 1994; Rao et al., 1991) in the Science Citation Index (ISI Web of Science). We also checked the reference lists of relevant articles, contacted experts and incorporated

suggestions proposed by the steering committee of the collaboration. We then selected the items we considered relevant to the settings represented in ART-LINC, formulated questions and organised them in different sections. We provided space to allow respondents to comment. The questionnaire was pilot tested and further changes were made.

The final version consisted of 140 close-ended and 54 open-ended questions relating to the site, the person completing the questionnaire and the prevention services and other relevant activities implemented by the programme. The content of the questionnaire, which is available on request, is summarised in Table 1.

Table 1. Content of questionnaire.

Topic	Total no of questions (no. of open-ended questions)
Contact information and characteristics of person completing questionnaire	6 (4)
Health education	
Content, type and staff involved	49 (7)
Psychosocial support	
Type of support, mode of delivery, staff involved	36 (11)
Disclosure, counselling and testing, and partner notification	
Support of disclosure, type of counselling and testing, procedures for partner notification	35 (8)
Prevention of mother-to-child transmission (PMTCT) and other interventions for special groups	
Protocols and drugs for PMTCT, breastfeeding, services targeted at special groups <sup>a</sup>	37 (13)
Provision of condoms and other contraception	
Male and female condoms, type of other contraception provided	12 (3)
Other questions	
Screening for sexually transmitted infections, activities to reduce stigma and discrimination of HIV-infected people, obstacles to implementing interventions	19 (8)

<sup>a</sup>Men who have sex with men (MSM), women, serodiscordant couples, ethnic minorities, immigrants, adolescents, intravenous drug users (IVDU), sex workers.

The questionnaire was implemented in September 2008 in DataCol (Data Collector), a web-based tool developed by WHO to create electronic surveys and forms (WHO, 2008a). The data are stored in a WHO-maintained database that is regularly backed up. Respondents downloaded the questionnaire as an executable file, completed it on-line or off-line and sent it back to the data centre at University of Bern.

### **Statistical analysis**

Answers to open-ended questions were summarised and coded where appropriate. We used univariable, unweighted logistic regression analysis to explore whether programme characteristics influenced the availability of preventive services. We considered the type of programme (government versus non-governmental organisations or private clinic), access to ART (free of charge versus fee-for-service) and work load (scale-up cohorts with rapid increase in patient numbers in recent years versus cohorts with stable patient numbers). Dependent variables were whether or not the programme had a protocol for partner notification, whether or not it routinely screened for sexually transmitted infections (STI) in asymptomatic patients and whether dedicated services for adolescents or serodiscordant couples were available. Most countries contributed one site only, which precluded analyses of country characteristics. Results are presented as number of sites (%) or odds ratios (ORs) with 95% confidence intervals (CIs). All analyses were done with STATA version 10 (Stata Corp; College Station, TX).

### **Results**

Twenty-two of 27 sites returned the questionnaire (response rate 82%). The questionnaire was completed by the clinical director in 15 sites (68%), by researchers in five sites (23%) and by clinic managers in two sites (9%). Nine respondents were female (41%) and 13 were male (59%).

The characteristics of sites are summarised in Table 2. Eight sites (36%) were located in South Africa, two in Brazil, two in Zambia and one each in Argentina, India, Thailand, Botswana, Ivory Coast, Malawi, Morocco, Uganda and Zimbabwe and one occupational programme of a brewery company included five countries (Nigeria, Republic of Congo, Democratic Republic of Congo, Rwanda and Burundi). This programme was standardised across sites and was therefore treated as a single site. All 22 sites were located in urban areas, 19 were specialised ART clinics and three sites (two occupational clinics and a private clinic) also functioned as

general practices. Sixteen programmes (73%) were public and government-funded and six were run by non-governmental organisations. Sixteen sites (73%) provided ART free of charge (Table 2). The five sites that did not participate included one smaller research cohort in Senegal and four scale-up cohorts in Botswana, Kenya, South Africa and Zambia.

### **Health education, condoms and other interventions**

Health education was provided by 21 of the 22 sites (96%). Table 3 details the topics covered: most programmes addressed the routes of transmission, prevention of sexual transmission by male condoms and prevention of mother-to-child transmission (PMTCT). Other topics, for example, female condoms, were covered by fewer programmes. Health education was delivered through talks in the waiting area (17 sites, 81%), posters (15 sites, 71%) and flyers (13 sites, 62%). Twenty-one sites (96%) provided male condoms and seven (32%) female condoms. Practical instructions on the correct use of male condoms were provided by 12 sites (57%) and on the use of female condoms by seven sites (33%). Condoms were generally available free of charge. Twelve sites (55%) provided injectable or oral contraceptives. All sites provided post-exposure prophylaxis (PEP) for staff, for example, after needle stick injuries. No site provided clean needles or syringes for intravenous drug users. Twenty-one sites (96%) tested for STI but only 12 of these (57%) screened asymptomatic patients at the first visit and seven (33%) screened at regular intervals. Twenty sites (91%) screened routinely for syphilis in pregnant women. Point of care testing for syphilis was available in 15 sites (68%) and same day treatment in nine of these 15 sites (60%).

Ten sites (46%) were involved in activities to reduce poverty in HIV-infected patients, including, for example, projects to generate income or support to access social security grants. One programme was involved in activities to reduce stigma associated with HIV in the community, through marches, radio talks, theatre or the distribution of T-shirts printed with the words "HIV-positive".

### **Disclosure, counselling and testing and partner notification**

All sites encouraged patients to disclose their HIV test result to partners and spouses. Twenty-one sites (96%) provided psychosocial support. This included counselling (21 sites, 100%), referral to self-help groups (17 sites, 81%) and drop-in centres (four sites, 19%). Issues addressed included financial problems, stress management, coping strategies and the strengthening

Table 2. Characteristics of the 22 antiretroviral therapy (ART) programmes included in the survey.

Region and country	Site	Start of ART provision	No. of HIV-infected patients	No. of patients on ART	Routine viral load monitoring	Public programme	Free access to ART	Scale-up cohort <sup>a</sup>
Asia								
Thailand	A	2003	1000	314	Yes	Yes	No	No
India	B	1996	10,000	5800	No	No	Mixed <sup>b</sup>	Yes
South America								
Argentina	C	2003	3200	2500	Yes	Yes	Yes	No
Brazil	D	1996	2500	1100	Yes	Yes	Yes	No
Brazil	E	1996	2200	1500	Yes	Yes	Yes	No
Africa								
Morocco	F		850	760	Yes	Yes	Yes	No
Côte d'Ivoire	G	1999	10,491	3393	No	No	No	Yes
Uganda	H	2001	6500	3300	Yes	Yes	Yes	No
Botswana	I	1990	3000	1750	Yes	No	No	No
Malawi	J	2002	7700	6284	No	Yes	Yes	Yes
Zambia	K	1997	300	100	Yes	No	No	No
	L	2003	1434	292	No	Yes	Yes	No
Zimbabwe	M	2004	1448	1157	No	Yes	Yes	No
South Africa	N	1996	4864	3065	Yes	Yes	No	Yes
	O	1999	13,349	10,119	Yes	Yes	Yes	Yes
	P	2004	979	939	Yes	Yes	Yes	No
	Q	2004	1350	683	Yes	No	Yes	No
	R	2001	6000	3000	Yes	Yes	Yes	Yes
	S	2002	3883	2400	Yes	Yes	Yes	Yes
	T	2004	1675	1133	Yes	Yes	Yes	No
	U	2003	1009	481	No	Yes	Yes	No
Sites in several countries <sup>c</sup>	V	2001	393	277	Yes	No	Yes	No
Median (range)		2001 (1996–2004)	2350 (300–13,349)	1328 (100–10,119)				
Number with characteristics (%)					16 (73%)	16 (73%)	16 (73%)	7 (32%)

<sup>a</sup>Sites with increasing patient numbers over several years were considered scale-up cohorts.<sup>b</sup>About 30% of patients have free access to ART.<sup>c</sup>Nigeria, Republic of Congo, Democratic Republic of Congo, Rwanda, Burundi.

Table 3. Topics covered in health education activities provided at 21 antiretroviral therapy (ART) programmes.

Topic	No. of sites (%) addressing topic
General information about the virus, course of the disease and therapy	21 (100%)
Routes of transmission	21 (100%)
Misperception about transmission	21 (100%)
Risk of transmission by unprotected sex	21 (100%)
Risk of transmission by having multiple sex partners	21 (100%)
Male condoms to prevent transmission	21 (100%)
Prevention of mother-to-child transmission (PMTCT)	20 (95.2%)
Risk of transmission through sex under the influence of alcohol and other substances	20 (95.2%)
Risk of transmission by blood transfusions	18 (85.7%)
Influence of antiretroviral therapy on transmission risk	18 (85.7%)
Abstinence to prevent transmission	18 (85.7%)
Monogamy to prevent transmission	17 (81.0%)
Contraception to prevent unplanned pregnancy	17 (81.0%)
Risk of transmission by needle sharing	16 (76.2%)
Female condoms to prevent transmission	15 (71.4%)
Role of post-exposure prophylaxis (PEP)	14 (66.7%)
Vaginal microbicides to prevent transmission	4 (19.0%)

Note: Table shows the number of sites that covered topic. Percentages relate to the 21 sites that provided health education. One out of 22 programmes did not provide health education.

of self-confidence. Eleven sites (52%) addressed gender-based violence. Counselling and testing was available on site in 18 (82%) programmes. This included voluntary counselling and testing (VCT) at 16 of the 18 sites (89%), couple counselling and testing in 15 sites (83%) and routine, opt-out, testing in pregnant women at 11 sites (61%). Eleven sites (50%) had a protocol for managing partner notification of HIV-infected people; most of them used the patient referral method, where patients themselves inform sexual partners and ask them to attend a clinic for counselling and testing. One site indicated that they used provider referral where the health professional contacts the partner on behalf of the patient, and two sites reported that they would inform partners if the patient had not done so after a certain period of time.

### ***Prevention of mother-to-child transmission (PMTCT) and other interventions targeted at specific groups***

Twenty sites (91%) provided ART to prevent mother-to-child transmission (Table 4). Regimens for the mother varied widely. Nine sites (41%) provided triple combination ART based on nevirapine (NVP) or efavirenz. Other regimens included zidovudine (AZT) from 28 weeks and single-dose NVP, dual therapy with AZT and lamivudine (3TC) and single-dose NVP in all women or in women with CD4 cell counts above 200 cells/ $\mu$ L. Similarly, in newborns, regimens included single-dose NVP, single-dose NVP and AZT for one week or one month. A minority of sites (8, 36%) recommended elective caesarean section.

Most programmes (19, 86%) recommended exclusive replacement feeding to prevent MTCT but over half of them (11 of 19, 58%) also recommended exclusive breastfeeding either followed by rapid

Table 4. Interventions offered or promoted by 22 antiretroviral therapy (ART) programmes to prevent mother to child transmission (MTCT) during pregnancy and birth, and after birth.

Measure	No. of sites (%) providing measure
Prevention of MTCT during pregnancy and birth	
Prophylactic antiretroviral therapy	20 (90.9%)
Promotion of hospital delivery	13 (59.1%)
Promotion of elective caesarean section	8 (36.4%)
No specific measures in place	2 (9.1%)
Prevention of MTCT during breastfeeding	
Promotion of exclusive replacement feeding <sup>a</sup>	19 (86.4%)
Promotion of six months exclusive breastfeeding followed by rapid weaning	7 (31.8%)
Promotion of six months exclusive breastfeeding followed by mixed feeding	5 (22.7%)
Provision of formula milk free of charge	13 (59.1%)
Heat-treating breast-milk	1 (4.5%)
Antiretroviral therapy during breastfeeding	1 (4.5%)
No specific measures in place	1 (4.5%)

<sup>a</sup>If acceptable, feasible, affordable, sustainable and safe. Eleven of these sites provided formula milk free of charge.

Note: Table shows the number of sites that provided the specific measure. Percentages relate to the 22 sites that participated in the survey. Interventions are not exclusive: a programme could promote several interventions.

weaning or complementary (mixed) feeding (Table 4). Eleven of the 19 programmes (58%) provided formula milk free of charge. With the exception of three sites in South Africa and Botswana, 12 of the 15 programmes in sub-Saharan Africa (80%) recommended six months of exclusive breastfeeding followed by complementary feeding (five sites) or rapid weaning (seven sites). Figure 1 shows the number of sites involved in preventive services targeted at different groups. In addition to PMTCT, 12 sites (55%) were involved in activities aimed at women or adolescents and 10 sites (46%) worked with serodiscordant couples. Few sites provided preventive services to other groups.

### *Determinants of provision of preventive services*

There were no statistically significant associations with programme characteristics. There was some evidence that partner notification protocols were less likely to be in place in programmes not funded through government (OR 0.39, 95% CI 0.06–2.8), in programmes that charged patients for ART (OR 0.12, 95% CI 0.01–1.29) and in scale-up programmes (OR 0.66, 95% CI 0.11–4.0). Regular screening for STI tended to be less likely in scale-up cohorts compared to other programmes (OR 0.30, 95% CI 0.03–3.3).

### *Obstacles*

In an open-ended question, respondents were asked to describe the main problems in implementing preventive services in their programme. The “background of stigma, discrimination, blame” (female respondent from Thailand) was considered a major problem in implementing prevention services and

similar comments were made by six other respondents from Argentina, India, South Africa and Zambia. Another recurring theme was the very high patient load “so there is often inadequate time for counseling” (female respondent from Zimbabwe) and financial constraints, “which prevent programmes from hiring additional staff” (male respondent from Côte d’Ivoire).

### **Discussion**

Preventive services for HIV-positive people were available in most of the ART programmes surveyed in this study. The programmes focused on health education aimed at changing behaviour of patients and the provision of social support, male condoms and of interventions to prevent transmission from mothers to their newborns and infants. Fewer sites had protocols for partner notification or offered specific interventions for discordant couples, adolescents and other groups at high risk. Moreover, only a minority of sites regularly screened for STI and only one site was involved in activities to reduce the stigma and discrimination associated with HIV infection.

Our survey predates the publication of WHO’s recommendations on essential prevention interventions (WHO, 2008b) but it covered many of the recommended interventions and may thus serve as a baseline to assess progress with integrating interventions in ART programmes. Our study has several limitations, however. The clinics and programmes that participate in ART-LINC of IeDEA are not representative of all sites providing ART in the countries studied, being mainly urban and having electronic databases for data capture (Forster et al., 2008). The provision of preventive services, or the lack thereof, was not, however, a criterion for inclusion in the ART-LINC collaboration. In addition, many of the countries that are scaling-up ART were represented in the survey. The data were self-reported and results might have been affected by social desirability bias. This seems unlikely considering that sites have been collaborating for several years and helped design the study. Finally, the quality of preventive services was not assessed.

Although VCT was provided by most sites, only a minority of programmes reported specific interventions targeted at discordant couples. Discordant couples represent an important target for HIV-1 prevention, particularly in sub-Saharan Africa, where most transmissions occur among discordant couples who are unaware of their serostatus (Gayle & Lange, 2004; Piot, Bartos, Larson, Zewdie, & Mane, 2008). ART programmes are in an ideal position to identify discordant couples and deliver interventions. A trial

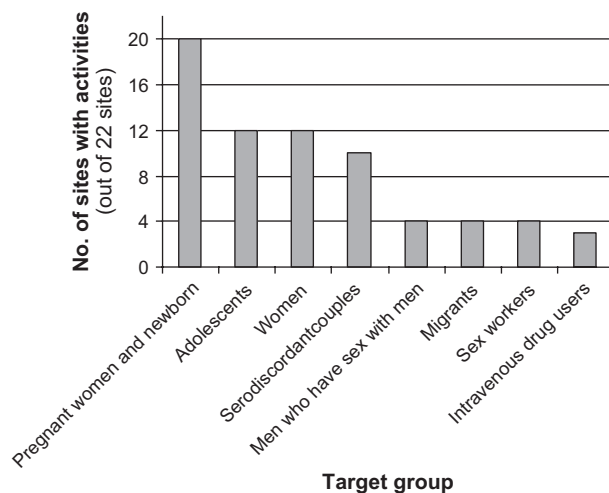


Figure 1. Number of sites involved in preventive services aimed at specific target groups.

in Kenya, Tanzania and Trinidad, which randomly assigned couples to VCT or basic health education, found that couples assigned to counselling and testing reduced unprotected intercourse more than couples assigned to health education (The Voluntary HIV-1 Counseling and Testing Efficacy Study Group, 2000).

Providing advice on disclosing to sexual partners is part of the testing and counselling process. There is therefore substantial overlap with partner notification, in which the partners of people with STI are informed of their exposure (Hogben, McNally, McPheeters, & Hutchinson, 2007; Mathews et al., 2001), but only half of programmes had protocols for partner notification. Partner notification for HIV infection has also been difficult to implement in industrialised countries, where it is sometimes viewed as a coercive public health intervention that conflicts with protecting the individual's right to privacy, especially before the widespread introduction of ART (Golden, Fixelid, & Low, 2008). The diagnosed person might experience negative events including relationship breakdown or physical violence (Grinstead, Gregorich, Choi, & Coates, 2001; Hogben et al., 2007). The terminology of personalised risk reduction in a client-centred approach might have facilitated the acceptance of VCT services for HIV infection. The benefits of involving patients with other STI in informing their partners are becoming increasingly recognised (Trelle, Shang, Nartey, Cassell, & Low, 2007). Sharing successful approaches to VCT and partner notification interventions may thus contribute to improving the control of all STI. Clearly, either intervention should only be offered if the support needed to help newly diagnosed people, and particularly women, to cope with their disease is also available. It is reassuring that most sites provided such support.

Few sites offered services that covered several or all components of PMTCT, including the prevention of infection in HIV-negative women, of unwanted pregnancies and of transmission to the offspring during pregnancy, birth and breastfeeding (Piot et al., 2008; Dabis & Ekpin, 2002). Only 12 sites (55%) provided contraception other than condoms. The prevention of unwanted pregnancies as an important primary prevention strategy does not appear to have been widely implemented. Also, recommendations and drug regimens for the prevention of transmission to neonates and infants varied widely. This may be a reflection of the complexity of current guidelines (WHO, 2006) but some of the variation must be of concern: not all sites systematically provided suppressive triple combination ART to pregnant women with indications for ART,

a strategy that is safe, highly effective and unequivocally recommended by WHO (WHO, 2006).

Our study is relevant to the debate on whether infants of HIV-infected women in resource-limited settings should be breastfed or formula fed (Coutsoudis, Goga, Rollins, & Coovadia, 2002; Mofenson & McIntyre, 2000). HIV transmission to infants occurs through breastfeeding but exclusive breastfeeding for the first few months of life is associated with lower transmission rates than is complementary feeding (Coovadia et al., 2007; Iliff et al., 2005). Formula feeding substantially increases the risk of death due to diarrhoea, acute respiratory infections and other infectious diseases (WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality, 2000). The updated WHO guidelines (WHO, 2007), therefore, stress that although formula feeding may be the right choice for some HIV-infected women, exclusive breastfeeding for the first six months is the gold standard for the babies of HIV-infected mothers who live in resource-poor settings and cannot supply replacement feeding safely (Coutsoudis, Coovadia, & Wilfert, 2008). In keeping with these guidelines recommendations and practices differed across sites, and differed within the same country, for example in South Africa, where large disparities in socio-economic status and infant mortality rates exist. It nevertheless appears that the updated guidelines may not yet have been widely implemented: nine sites (41%) promoted rapid weaning, which is not recommended by the guidelines (WHO, 2007).

Our respondents stressed that stigma and discrimination at the level of the community, high patient load and financial constraints were important obstacles for the implementation of preventive services in ART programmes. The Global HIV Prevention Working Group (Gayle & Lange, 2004) and other agencies have argued that staff of ART programmes should be trained to deliver prevention services. In particular, ART programmes should actively address and reduce discrimination of HIV-infected people in the communities they serve. Piot and colleagues called for a coalition of youth, women's and religious organisations, as well as business leaders and HIV/AIDS activists to create a newly energised HIV prevention movement (Piot et al., 2008). By making effective treatment and appropriate prevention services available, ART programmes can make important contributions to both prevention and the expansion of access to ART. Treatment programmes should not operate in isolation but need to be part of, and supported by, the prevention constituency.



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